March 19, 2015

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers lane, Rm. 1601
Rockville, MD 20852

Re:

Modified Risk Tobacco Product Applications for 10 brands of snuss submitted by Swedish

Match North America, Inc.

From: Gregory N Connolly DMD, MPH
Research Professor Northeastern University School of Law and Bouve School of Health Sciences

We wish to go on record in opposition to the proposed approval of Swedish Match North America's (SMNA) request to have a 10 Snuss brands approved as Modified Risk Tobacco Products (MRTPs) under Section 911 of the Family Smoking Prevention and Tobacco Control Act (FSPTCA) based on violations of the Section 911 of the FSTPCA, inapplicability of the applications to the US market, the shortcomings of the evidence submitted and the questionable science on the impact of availability of Snuss being causally related to the decline in male smoking prevalence.

We strongly believe that FDA should immediately proceed to establish a tobacco product standard under section 907 for all brands of oral smokeless tobacco for Tobacco specific nitrosamines in particular for NNN and NNK the principle suspected carcinogens in oral smokeless tobaccos.

The basis of our opposition is as follows:

1.) The SMNA MRTP applications violate Section 911 and Congressional intent by relying on "Best Practical Standards" (Gothia Technique) a commercial standard for reducing toxicants and implying such standards are based on scientific evidence. Scientific standard have already been established by federal regulatory agencies for many of the toxicants at levels of magnitudes lower than those found in the applications and a TPSAC recommendation for approval to FDA would set a dangerous precedent for tobacco products standard setting, undermine broad federal efforts to protect the public health be based science and not marketplace needs.

The SMNA applications rely heavily on the Gothia Tek standard, a method developed by SMNA parent company Swedish Match, to reduce the levels of known toxins in oral smokeless tobacco to levels lower than in other oral smokeless tobacco products based on best technical practices. The assumption is that these reductions would reduce disease risks in particular cancer. However, the applications contained no scientific evidence demonstrating disease risk threshold for the lower levels based on scientific research. Simply lowering concentrations even by 50% of toxins such as tobacco specific nitrosamines is based on commercial feasibility and not scientific evidence that violates Section 911(g)(1) . According to this section, two considerations shall be considered based on the applicant demonstrating that the MRTP will

"Significantly reduce harm and the risk of tobacco-related disease to individual users of tobacco users: and

Benefit the health of the population as a whole taking in to account both users of tobacco products and persons who do not currently use tobacco products (Section 911 (h) (5) of the FD&C Act. Section 911(g)(1) allows FDA to issue an order under 911(g)(2) of the FSTPCA, FDA may issue and approval order for applications if the applicant has demonstrated."

Section 911(g)(1) establishes methods to respond to these requirement to issue an order under 911(g)(2) of the FSTPCA including:

> 2.) "Scientific evidence is not available and, using the best available scientific methods, cannot be made available without conducting long-term epidemiological studies for an application to meet the standards for obtaining an order under section 911(g)(1)"
> 3.) "The scientific that is available without conducting long-term epidemiological studies demonstrates that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonable likely in subsequent studies."

In both cases Congress clearly limits the type of evidence for approval to scientific evidence and gives FDA no authority to approve MRTP applications on levels based on commercial feasibility "best technical manufacturing practices.

Congress does allow "Technical Achievability" submissions to be considered in setting tobacco products standards under S 907 under which TPSAC reviewed and made recommendations for menthol. Congress stated in S 907:

> S 907(b) (1) ""Technical Achievability". The Secretary (FDA) shall consider information submitted in connection with as proposed standard regarding the technical achievability of compliance with such an order."

We recommend that these applications be rejected and the Law maintained by FDA setting a tobacco product standard for tobacco product nitrosamines for all oral smokeless tobacco products based on science but allowing consideration of submissions of "Technical Achievability".

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these reductions would reduce disease risks in particular cancer. However, the applications contained no scientific evidence demonstrating disease risk threshold for the lower levels based on scientific research. Simply lowering concentrations even by 50% of toxins and not on scientific evidence Section 911(g)(1) is violated.

In simple terms, this means if the current manufacturing processes do not allow the reduction of the level of toxicants to what the science requires this clinical evidence as recommended in the Institute of Medicine Report of 2012 as essential to MRTP approvals is in error.

No such wording appears in S 911 clearly showing that Congress did not extend this authority to S 911 and MRTP orders. Under S 911, FDA cannot approve an application that basis a large portion of its clinical evidence on best technical practices. In the MRTP applications over 50 pages are submitted on the levels of biomarkers of exposure or harm (sections 6.1.4 through 6.1.4.2.2 pages 495 through 547).

Given the multiple toxicants in the list, many of which are known carcinogens, a simple dose relationship cannot be assumed if a tolerance limit for cancer effects have already been established at far lower levels than that proposed even by a 50% or more. In correspondence with SM's Executive Vice President Eric Lindquist in 2009 in response to our request for scientific evidence showing that a reduction of toxicants to the levels proposed in the Gothia Tek reduced risk of disease he responded:

> "Our voluntary Gothia Tek standard…was developed …taking into account practice and science". "Much could be gained from a more unified vision and strategy to guide research and policy in this area".

No scientific evidence was supplied in the response and appendix A contains our request and SW's response. (See appendix A)

Federal regualtory agencies such as the FDA have set scietific standards for many of the toxicants identified in the applications which are of magnitudes lower than that of the the Gothia Tek standard. FDA and USDA have already set a tolerance limit of one nitrosamine, a group of potent carcinogens with high concentrations of tobacco specific nitrosamines of NNK and NN in oral smokeless tobacco, to 5 ng/g for baby bottle nipples, beer or bacon. The level reccommened in the MTP applactions for NNN and NNK combined are 1 ug/g or 200 times greater that that already established by the FDA or USDA.

In order to better understand cancer risk these the Gothia Tek standards differences in scieicne based and best technncal practices vcality bsdd TSNAs and other toxicants for

Based on these criteria we have reviewed the Swedish Match North American (SWNA) Modified Risk Tobacco Product (MRTP) applications for the 10 snuss brands and the SMNA submission by SMNA reviewing research on the individual health effects and population impact of Swedish snuss on youth initiation and dual use among other population effects. Based on this review we conclude that SWNA, the applicant, has failed to submit sufficient information for the FDA to determine that the two considerations have been scenically met particularly of the United States tobacco market.

Applying toxicological risk assessment principles to constituents of smokeless tobacco products: implications for product regulation, Olalekan A. Ayo-Yusuf and Gregory N. Connolly, Tobacco Control 2011 20: 5357 originally published on line October 5, 2010. (doi: 10. 1136/tc.2010.037135) We determine how information on chemical constituents of different smokeless tobacco products (STPs) may be used in cancer risk assessment for regulatory purposes. We investigated selected STP constituents potentially associated with significant cancer risk that also appeared on the Gothia Tek standards.

We applied known toxicological risk assessment frameworks. Cancer risk estimates were obtained for selected constituents of STPs and a medicinal nicotine gum formulation with comparable toxicity information and also median concentration data on the Gothia Tek analytes. The calculated cancer risk was considered 'unacceptable' if it exceeded the US Environmental Protection Agency's (USEPA's) benchmark of an 'acceptable' cancer risk of 10E 6. The cancer risk estimates derived from daily use of 10 g of STPs meeting the industry-set Gothia Tek limits exceeded the levels generally considered 'acceptable' by the USEPA at least 8000 times. Table 1 Calculated cancer risk for selected smokeless tobacco product (STP) constituents meeting Gothia Tek standards. Table 1 summarizes the results

Table 1 Calculated cancer risk for selected smokeless tobacco product (STP) constituents meeting GothiaTek standards

Compound	GothiaTek limit (ng/g dry weight)	Laboratoryz method detection limit (ng/g dry weight)	Compound TD_{50} (mg/kg body weight/day)	Cancer potency factor ((mg/kg body weight/day)^{L1})	Cancer risk estimate (100% transfer)	Cancer risk estimate (reduced percentage transfer)
TSNA*	10000	230x	0.0999	10.1	6.2310E3	5.3310E3
BaP (BaPeq)y	20 (40)y	0.04	0.956	1.1	2.7310E6	1.6310E7
Cadmium	1000	43.3	0.0217	46.1	2.8310E3	1.7310E4
Lead	2000	37.9	46.6	0.02		
Arsenic	500	25	No comparable CPDB data		2.5310E6	1.5310E7
Chromium	3000	11.9	No comparable CPDB data			
Product total risk					9.0310E3	8.1310E3

*TD_{50} (chronic dose rate in mg/kg body weight/day, which would induce tumours in half the test animals at the end of a standard lifespan for the species) for NNK and NNN was used as a conservative estimate of risk for the composite of TSNAs and 85% bioavailability was assumed for each when calculating reduced percentage transfer.[24] yCancer risk estimates were based on concentrations using BaP equivalents (BaPeq) to represent contributions from other carcinogenic PAHs. zThese are detection limits for the selected constituents in processed tobacco as reported by the laboratory that tested the STPs used in this study.

xThis was based on the analysis of the tobacco 'as received'.

BaP, benzo(a)pyrene; CPDB, carcinogenic potency database; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN, N'-nitrosonornicotine; PAH, polycyclic aromatic hydrocarbon; TSNA,
tobacco specific nitrosamine.

*We used the rat TD50 for NNK & NNN as a conservative estimate of risk for composite of TSNAs and assumed 17% bioavailability each (Hecht et al., 2008).
Except for the medicinal nicotine tested, all the STP types, including the relatively lower tobacco specific nitrosamine (TSNA)-containing snus, were found to carry an 'unacceptable' cancer risk.

The calculated cancer risks associated with the snus and the US moist snuff products were, respectively, at least 1000 times and 6000 times greater than the minimum acceptable. TSNA and cadmium are associated with the largest estimated cancer risks for all the STPs evaluated. This study's findings provide an empirical risk assessment that provides sufficient evidence to determine that the MRTP applications have failed to provide the FDA with comparable sufficient risk assessment data on constituents of the MRTP application to determine the criteria are met.

2.) The Vast majority or evidence contained in the MRTP applications and the retail handling of Snuss is from Sweden or other nations and not the US.

The MRTP submissions on dual use perhaps the greatest concern of smokeless tobacco in having and adverse impact on public health provide only 2 paragraphs on the US experience with dual use and smokeless tobacco versus dozens of pages on Swedish studies that may not be applicable to the United States market. A number of studies have found high dual use patterns among adolescents white males particularly from the Southeast and Southwest of the United States which are better addressed in other submissions.

In Sweden Snuss is routinely refrigerated in retail outlets to prevent "TSNA Aging" where additional levels of TSNAs are formed in the tin if held at room temperature. SM is known to cover the costs of the refrigerators but in nowhere is this stated for the US market.

3.) While SWNA will lower the toxicants levels for 10 selected brands of snuss, SWNA does not propose reducing levels of toxins in their oral smokeless tobacco brands sold in the US previously held by Pinkerton Tobacco Company acquired by SMNA such as Timberwolf, Longhorn and others. SMNA oral smokeless tobacco brands make up make up 19% of the US oral tobacco market. Nor will SWNA lower all levels of toxicants that SM has done in Sweden. Sweden will maintain stronger package warnings than the US if approved and have only one low level of toxicants.

This is of major concern since the varied toxicant levels along with the proposed warning labels will set dual standards for oral smokeless tobacco in the US with unknown effects on the public health not addressed in the MRTP applications.

In our 2006 study of nicotine and TSNAs levels done by Labstat of Canada levels of SMNA Long Horn and Timber Wolf brands averaged 5,015 ug/g far greater than that proposed for

the MRTPs. This dual treatment of US consumers versus Swedish consumers raises serious questions about the corporate responsibility of SMNA.

In Sweden oral smokeless tobacco brands bear the warning label:

"This package can damage your health and is addictive."

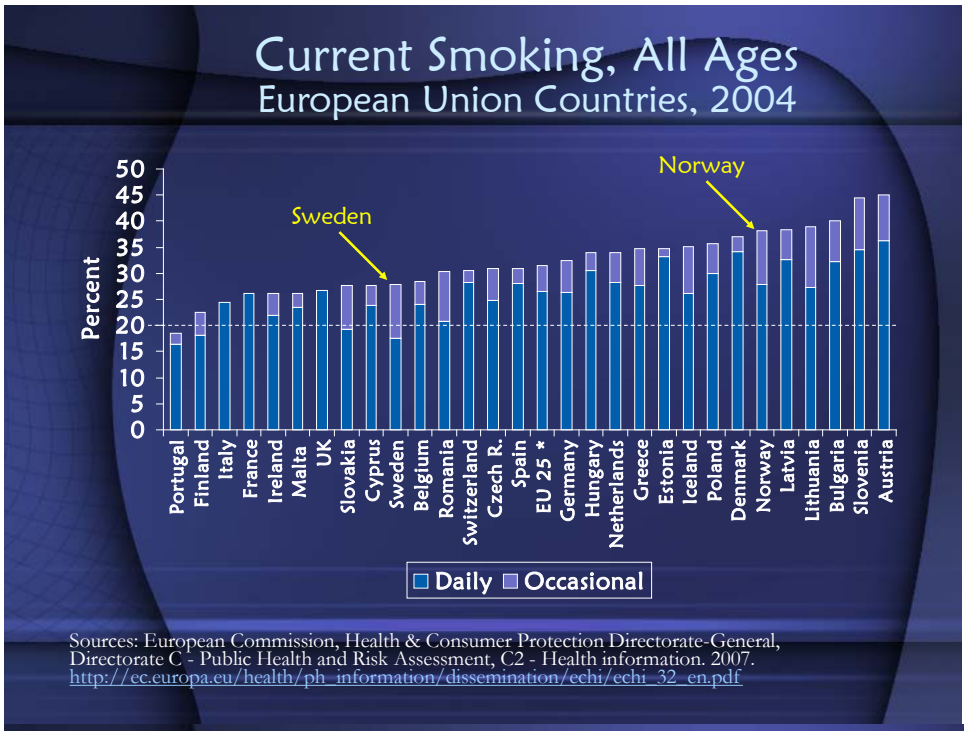
The proposed US label for the same brands proposed by SWNA is far weaker:

"No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes" "Warning: Smokeless tobacco is addictive".

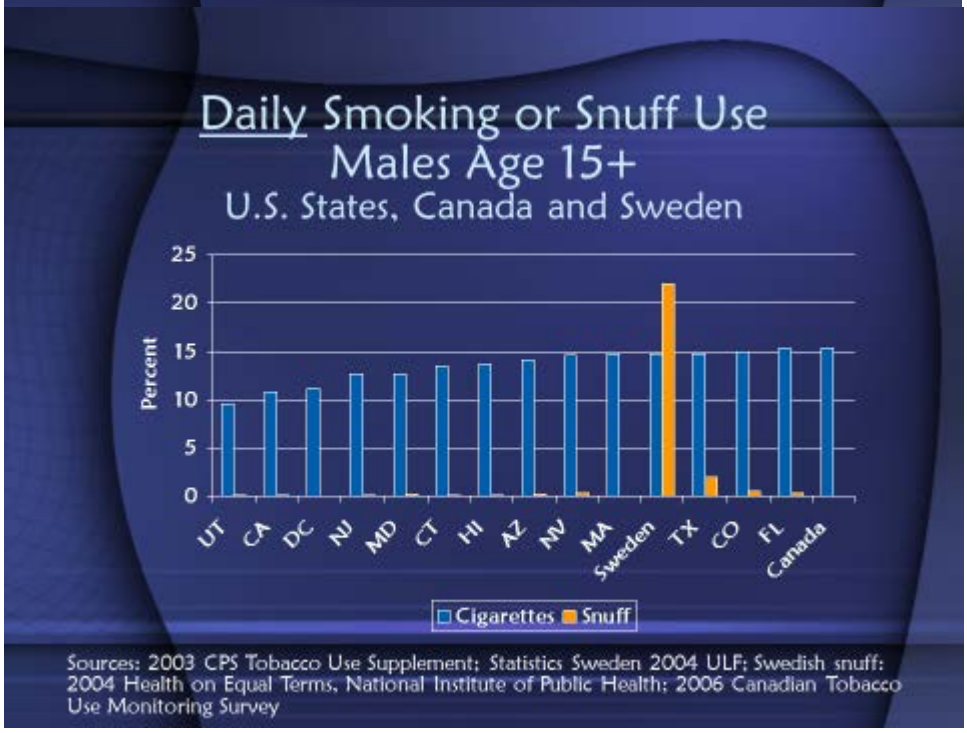
4.) A major claim made in the MRTP submissions is that the availability of oral smokeless tobacco contributed to a significant decline in male smoking prevalence and male lung cancer. The studies referenced do not control for the impact of one of the world's most aggressive public health campaigns that of Sweden nor provide controls, jurisdictions with similar demographics that have little or no oral smokeless tobacco use. Although suggestive of a relationship it is our opinion that is it proven to be not causal.

The Swedish Ministry of Health was one of the Ministries in any nations to introduce a comprehensive tobacco control campaign with strong package warnings, clean indoor air campaigns, very high cigarette taxes, strong community based tobacco control campaigns and was one of the first nations to approve smoking cessation medications. The effect of this campaign deserves far more credit in the reduction of male smoking than the actions of a tobacco company.

A comparison of control jurisdictions including many US states show lower levels of smoking prevalence than Sweden and in some (Massachusetts) no detectable levels of smokeless tobacco use. The World Health Organization's Study Panel on Smokeless Tobacco recommended that nations with no use of oral smokeless tobacco ban use before use becomes widespread. The European Union has banned oral smokeless tobaccos exempting Sweden when it joined the EU as has Australia, New Zealand, Taiwan, and others.



Sources: European Commission, Health & Consumer Protection Directorate-General, Directorate C - Public Health and Risk Assessment, C2 - Health information. 2007.
http://ec.europa.eu/health/ph_information/dissemination/echi/echi_32_en.pdf



Sources: 2003 CPS Tobacco Use Supplement; Statistics Sweden 2004 ULF; Swedish snuff: 2004 Health on Equal Terms, National Institute of Public Health; 2006 Canadian Tobacco Use Monitoring Survey

5.) Numerous clinical and epidemiological studies done primarily done in in Sweden raise serious

Questions about the relative safety of Snuss. Little research has been done on the effects of many toxins such as heavy metals based on the recent increase in use and unknown systemic effects.

The following summaries of these various studies raise serious concerns and warrant that the principle of prevention, long practiced by FDA, serve as a guide to assessment of relative risks between snuss and smoking. Metal contaminant assessment levels for other products are presented to high light the need for such caution.

Specific Toxicants

Heavy Metals

Toxic heavy metals are found in tobacco products and may contribute to cancer and non-cancer (e.g. heart disease) outcomes. Cadmium, lead, chromium, nickel, arsenic, and mercury were detected in all products, while no products contained quantifiable levels of selenium. Chromium levels were highest among all metals detected for all products followed by nickel. Levels of mercury were lowest for all products among quantifiable metals (Table 5).

Metal Contaminant Acceptance Levels

Heavy metals are known to cause health effects at various stages of life, including cancer, and particular susceptibility to neurobiological effects in the fetus and during developmental stages of life. A number of heavy metal constituents have been found in smokeless tobacco and tobacco in all forms. These include arsenic (As), cadmium (Cd), chromium (Cr), cobalt (Co), lead (Pb), mercury (Hg), and nickel (Ni), and others. Primary sources for regulatory values and guidelines include the U.S. Food and Drug Administration (FDA), U.S. Environmental Protection Agency (USEPA), Joint Food and Agricultural Organization / World Health Organization Expert Committee on Food Additives (JEFCA), U.S. Agency for Toxic Substances and Disease Registry (ATSDR), California's Safe Drinking Water and Toxic Enforcement Act of 1986, and American National Standards Institute (ANSI) National Sanitation Foundation (NSF). The basis of the calculations for the acceptable or tolerable levels of the metals in the finished product follows a mathematical model in which an acceptable or tolerable daily intake in mg/kg body weight is multiplied by the average mass of an adult (60 or 65 kg for women, and 70 or 75 kg for men).

Arsenic

The NSF recommends an acceptable daily intake of 0.01 mg per day in finished products containing arsenic based on JECFA provisional maximum tolerable weekly intake of 0.015 mg per kg body weight. The USEPA IRIS toxicological review of arsenic determined an oral RfD of 0.0003 mg per kg of body weight per day based on a NOAEL of 0.0008 mg per kg body weight per day in humans and an uncertainty factor of three. The FDA regulates the concentration of arsenic in bottled water and allows a maximum level of 10 µg / L. (21 CFR 165.110(b)(4)(iii)(A)). California's Safe Drinking Water and Toxic Enforcement Act of 1986 lists arsenic as a carcinogen with a no-significant risk level of 0.06 µg per day for routes of exposure other than inhalation.

Cadmium

The NSF recommends an acceptable daily intake of 0.06 mg cadmium per day in finished products based on JECFA provisional maximum tolerable weekly intake of 0.007 mg per kg body weight. The USEPA set a reference dose of 0.005 mg per kg body weight per day for food and water based on a NOAEL of 0.01 mg per kg body weight per day and an uncertainty factor of 10. The FDA set a level of 0.005 mg per L cadmium allowed in bottle water (21 CFR 103.35) and 0.05 ppm for amount of cadmium allowable in zinc methione sulfate tablets. The ATSDR set a minimum risk level for cadmium at 0.0002 mg per kg body weight per day.

Chromium

The NSF recommends an acceptable daily intake of 0.18 mg chromium based on the EPA oral reference dose (RfD) of 0.003 mg per kg body weight per day. The USEPA set an RfD of 0.003 mg per kg body weight per day for chromium. The FDA set a reference daily intake for chromium of 120 µg per day based on adult exposures and found inadequate data appropriate for use in determining recommended chromium exposures for children. ATSDR draft toxicological profile for chromium derives an oral minimum risk level (MRL) of 0.005 mg chromium (VI) per

kg body weight per day for intermediate exposure 0.001 mg chromium (VI) per kg body weight per day for chronic exposure.

Lead

The NSF recommends a tolerable daily intake of 0.24 mg lead based on JECFA provisional maximum tolerable weekly intake of 0.025 mg per kg body weight. The USEPA has considered deriving an oral RfD for inorganic to be in appropriate due to the harmful effects occurring at blood levels for which a threshold could not be established. The USEPA set an action level of 0.015 mg per L in the 90^{th} percentile of first-draw tap water samples. The FDA derived provisional tolerable intake levels of lead at 25 µg per day for pregnant women and 6 µg per day for infants.

Mercury

The NSF recommends an acceptable daily intake of inorganic mercury of 0.02 mg based on the USEPA RfD of 0.0003 mg per kg body weight per day.

Cobalt

The ATSDR derived an MRL of 0.01 mg cobalt/kg-day for intermediate-duration oral exposure. Based on the information supplied above and the heavy metal concentrations in dissolvable products, much more research needs to be done on how dissolvables levels match against those established by scientific agencies.

Physical Health Effects

Pancreatic and Oral Cancer

The International Agency on Cancer Research in 2008 concluded that smokeless tobacco causes oral and pancreatic cancer regardless of type.

International Agency for Research on Cancer. Monograph 89: Smokeless Tobacco and Some Tobacco specific N-Nitrosamines, 2007.

http://monographs.iarc.fr/ENG/Monographs/vol89/index.php; summarized in:

Cogliano V, Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F. Smokeless tobacco and tobacco-related nitrosamines. Lancet Oncol. 2004 Dec;5(12):708.

Many types of smokeless tobacco are marketed for oral or nasal use, and all contain different amounts of nicotine and nitrosamines. Overall, there is sufficient evidence that smokeless tobacco causes oral cancer and pancreatic cancer in humans, and sufficient evidence of carcinogenicity from animal studies. Tobacco-specific nitrosamines such as N'-nitrosonornicotine (NNN), 4-(methylnitrosamino)-l-(3-pyridyl)-1-butanone (NNK), N'-nitrosoanatabine (NAT), and iST-nitrosoanabasine (NAB), form by the nitrosation of nicotine

and other tobacco alkaloids. Substantial quantities form during the curing and processing of tobacco. Our Center's Tobacco Control Working Group concluded that exposure to NNN and NNK is "carcinogenic to humans" on the basis of sufficient evidence from animals and strong mechanistic evidence in exposed humans.

Fetal and neonatal effects: research on Swedish snus which is similar to dissolvables in design, shows a high risk to adverse fetal health

Relationship of Maternal Snuff Use and Cigarette Smoking With Neonatal Apnea. Gunnerbeck A, Wikström AK, Bonamy AK, Wickström R, Cnattingius S. Pediatrics. 2011 Aug 28. [Epub ahead of print]

Compared with infants of non-tobacco users, infants with prenatal exposure to snuff were at an increased risk of apnea even after adjustment for differences in gestational age (odds ratio: 1.96 [95% confidence interval: [1.30-2.96]). Smoking was associated with increased risk of apnea before, but not after, adjusting for gestational age.

Conclusions: Snuff use during pregnancy is associated with a higher risk of neonatal apnea than smoking. Maternal use of snuff or nicotine-replacement therapy cannot be regarded as an alternative to smoking during pregnancy.

Effect of Swedish snuff (snus) on preterm birth. Wikström AK, Cnattingius S, Galanti MR, Kieler H, Stephansson O. BJOG. 2010 Jul;117(8):1005-10

Compared with non-tobacco users, snuff users had increased risks of both very (adjusted OR 1.38; 95% CI 1.04-1.83) and moderately (adjusted OR 1.25; 95% CI 1.12-1.40) preterm birth. Compared with non-tobacco users, light smokers had increased risks of both very (adjusted OR 1.60; 95% CI 1.42-1.81) and moderately (adjusted OR: 1.18; 95% CI: 1.12-1.24) preterm birth, and heavy smokers had even higher risks. Among smokers, but not among snuff users, the risk was more pronounced for spontaneous than induced preterm birth.

Conclusions: The use of Swedish snuff was associated with increased risks of very and moderately preterm birth with both spontaneous and induced onsets. Swedish snuff is not a safe alternative to cigarette smoking during pregnancy.

Maternal smokeless tobacco use in Alaska Native women and singleton infant birth size. England LJ, Kim SY, Shapiro-Mendoza CK, Wilson HG, Kendrick JS, Satten GA, Lewis CA, Whittern P, Tucker MJ, Callaghan WM. Acta Obstet Gynecol Scand. 2011 Sep 9. doi: 10.1111/j.1600-0412.2011.01273.x. [Epub ahead of print]

After adjustment for gestational age and other potential confounders, the mean birth weight of infants of smokeless tobacco users was reduced by 78g compared with that of infants of non-users ($p=0.18$), and by 331g in infants of smokers ($p<0.01$). No association was found between maternal smokeless tobacco use and infant length or infant head circumference.

Conclusions: We found a modest but non-significant reduction in the birth weight of infants of smokeless tobacco users compared with infants of tobacco non-users. Because smokeless

tobacco contains many toxic compounds that could affect other pregnancy outcomes, results of this study should not be construed to mean that smokeless tobacco use is safe during pregnancy.

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Results: Compared with non-tobacco users, snuff users had increased risks of both very (adjusted OR 1.38; 95% CI 1.04-1.83) and moderately (adjusted OR 1.25; 95% CI 1.12-1.40) preterm birth. Compared with non-tobacco users, light smokers had increased risks of both very (adjusted OR 1.60; 95% CI 1.42-1.81) and moderately (adjusted OR: 1.18; 95% CI: 1.12-1.24) preterm birth, and heavy smokers had even higher risks. Among smokers, but not among snuff users, the risk was more pronounced for spontaneous than induced preterm birth.

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. **Pregnancy**

Compared with non-tobacco users, women who used snuff in early pregnancy had an adjusted odds ratio (OR) for pre-eclampsia of 1.11 (95% CI: 0.97 to 1.28). The corresponding ORs for light and heavy smokers were 0.66 (95% CI: 0.61 to 0.71) and 0.51 (95% CI: 0.44 to 0.58) respectively, with ORs lower for term than preterm pre-eclampsia. Compared with non-tobacco users, women who smoked in early pregnancy but had quit smoking before late pregnancy (weeks 30 to 32) had an adjusted OR for term pre-eclampsia of 0.94 (95% CI: 0.83 to 1.08). The corresponding OR for women who did not use tobacco in early pregnancy but had started to smoke before late pregnancy was 0.65 (95% CI: 0.50 to 0.85). We conclude that tobacco combustion products rather than nicotine are the probable protective ingredients against pre-eclampsia in cigarette smoke.

Non-cigarette tobacco use among women and adverse pregnancy outcomes. England LJ, Kim SY, Tomar SL, Ray CS, Gupta PC, Eissenberg T, Cnattingius S, Bernert JT, Tita AT, Winn DM, Djordjevic MV, Lambe M, Stamilio D, Chipato T, Tolosa JE. Acta Obstet Gynecol Scand. 2010;89(4):454-64.

Although cigarette smoking remains the most prevalent form of tobacco use in girls and in women of reproductive age globally, use of non-cigarette forms of tobacco is prevalent or gaining in popularity in many parts of the world, especially in low- and middle-income countries. Sparse but growing evidence suggests that the use of some non-cigarette tobacco products during pregnancy increases the risk of adverse pregnancy outcomes.

Cardiovascular Disease:

Recent research from Sweden raises serious concerns about use of snus and possibly dissolvables given their similarities to cardiovascular disease

Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. Bolindar G, Alfredsson L, Englund A, de Faire U. Am J Public Health. 1994 Mar;84(3):399-404.

The study population comprised 6,297 smokeless tobacco users, 14,983 smokers of fewer than 15 cigarettes per day, 13,518 smokers of 15 or more cigarettes per day, 17,437 ex-smokers, 50,255 other tobacco users, and 32,546 nonusers. Results: The age-adjusted relative risk of dying from cardiovascular disease was 1.4 for smokeless tobacco users and 1.9 for smokers of 15 or more cigarettes per day compared with nonusers. Among men aged 35 through 54 years at the start of follow-up, the relative risk was 2.1 for smokeless tobacco users and 3.2 for smokers. When data were adjusted for body mass index, blood pressure, and history of heart symptoms, the results were essentially unchanged. Cancer mortality was not raised in smokeless tobacco users. Both smokeless tobacco users and smokers face a higher risk of dying from cardiovascular disease than nonusers. Although the risk is lower for smokeless tobacco users than for smokers, the excess risk gives cause for preventive actions. Smokeless tobacco (snus) and risk of heart failure: results from two Swedish cohorts.

Arefalk G, Hergens MP, Ingelsson E, Arnlöv J, Michaëlsson K, Lind L, Ye W, Nyrén O, Lambe M, Sundström J. Eur J Cardiovasc Prev Rehabil. 2011 Aug 9. [Epub ahead of print]

Two independent Swedish prospective cohorts provided valuable information on the risk of cardiovascular disease. The Uppsala Longitudinal Study of Adult Men (ULSAM) involved a community-based sample of 1076 elderly men and the Construction Workers Cohort Study (CWC) involved a sample of 118,425 never-smoking male construction workers. In ULSAM, 95 men were hospitalized for heart failure during a median follow up of 8.9 years. In a model adjusted for established risk factors including past and present smoking exposure, current snus use was associated with a higher risk of heart failure [hazard ratio (HR) 2.08, 95% confidence interval (CI) 1.03-4.22] relative to non-use. Snus use was particularly associated with risk of non-ischemic heart failure (HR 2.55, 95% CI 1.12-5.82). In CWC, 545 men were hospitalized for heart failure during a median follow up of 18 years. In multivariable-adjusted models, current snus use was moderately associated with a higher risk of heart failure (HR 1.28, 95% CI 1.00-1.64) and non-ischemic heart failure (HR 1.28, 95% CI 0.97-1.68) relative to never tobacco use. Data from two independent cohorts suggest that use of snus may be associated with a higher risk of heart failure.

Risk of incident cardiovascular disease among users of smokeless tobacco in the Atherosclerosis Risk in Communities (ARIC) study. Yatsuya H, Folsom AR; ARIC Investigators. Am J Epidemiol. 2010 Sep 1;172(5):600-5.

The authors examined whether current use of smokeless tobacco was associated with increased incidence of cardiovascular disease (CVD) in 14,498 men and women aged 45-64 years at baseline (1987-1989) in the Atherosclerosis Risk in Communities (ARIC) Study. There were 2,572 incident CVD events (myocardial infarction, coronary revascularization, coronary death, or stroke) during a median of 16.7 years of follow-up (maximum = 19.1 years). Current use of smokeless tobacco at baseline was associated with 1.27-fold greater CVD incidence (95% confidence interval: 1.06, 1.52) than was nonuse, independently of demographic, socioeconomic, and lifestyle and other tobacco-related variables. Past use of smokeless tobacco was not associated with CVD incidence.

In conclusion, current use of smokeless tobacco was associated with increased risk of CVD incidence in ARIC cigarette nonsmokers. Current users of smokeless tobacco should be informed of its harm and advised to quit the practice. Current cigarette smokers should also be given sufficient information on safe, therapeutic methods of quitting which do not include switching to smokeless tobacco.

Smokeless tobacco and the risk of stroke. Hergens MP, Lambe M, Pershagen G, Terent A, Ye W. Epidemiology. 2008 Nov;19(6):794-9.

Information on tobacco use was collected by questionnaire among Swedish construction workers attending health check-ups between 1978 and 1993. In total, 118,465 never-smoking men without a history of stroke were followed through 2003. They used the Inpatient Register and Causes of Death Register to identify subsequent morbidity and mortality from stroke and its

subtypes (ischemic, hemorrhagic, and unspecified stroke). Almost 30% of the nonsmoking men had ever used snuff. Overall, 3248 cases of stroke were identified during follow-up. Compared with nonusers of tobacco, the multivariable-adjusted relative risks for ever-users of snuff were 1.02 (95% confidence interval; 0.92-1.13) for all cases and 1.27 (0.92-1.76) for fatal cases. Further analyses on subtypes of stroke revealed an increased risk of fatal ischemic stroke associated with current snuff use (1.72; 1.06-2.78), whereas no increased risk was noted for hemorrhagic stroke. Snuff use may elevate the risk of fatal stroke, and particularly of fatal ischemic stroke.

Risk of hypertension amongst Swedish male snuff users: a prospective study. Hergens MP, Lambe M, Pershagen G, Ye W. J Intern Med. 2008 Aug;264(2):187-94.

This examined the risk of hypertension in relation to long-term use of snuff based on longitudinal data. Repeated health check-ups were offered to all employees in the Swedish construction industry between 1978 and 1993. Blood pressure was measured at the health check-up and information on tobacco use and other risk factors was collected through questionnaires. In total, 120 930 never smoking men with information on blood pressure and snuff use at baseline were included. The association of high blood pressure and snuff use at baseline was estimated by logistic regression. Further, 42 055 men were identified as normotensive at baseline and had at least one subsequent health check-up. Through repeated blood pressure measurements and linkage to the Swedish National Inpatient Register, information on hypertension was obtained. Almost 30% of all men had used snuff. The adjusted odds ratio of high blood pressure amongst snuff users at baseline was 1.23 (95% CI 1.15-1.33) compared to never snuff users. The relative risk of high blood pressure during follow-up was 1.39 (95% CI 1.08-1.79) amongst snuff users and 1.36 (95% CI 1.07-1.72) for hypertension as recorded in the Inpatient Register. Conclusion: Use of Swedish moist snuff appears to be associated with a moderately increased risk of hypertension.

Long-term use of Swedish moist snuff and the risk of myocardial infarction amongst men. Hergens MP, Alfredsson L, Bolinder G, Lambe M, Pershagen G, Ye W. J Intern Med. 2007 Sep;262(3):351-9.

This study examined whether long-term use of snuff affects the risk of myocardial infarction. Between 1978 and 1993 all construction workers in Sweden were offered repeated health check-ups by the Swedish Construction Industry's Organization for Working Environment Safety and Health. A cohort was created with information on tobacco use and other risk factors, collected through questionnaires.

Setting: In total, 118,395 nonsmoking men without a history of myocardial infarction were followed through 2004. Information on myocardial infarction morbidity and mortality was obtained from national registers. Almost 30% of the men had used snuff. In total, 118,395 nonsmoking men without a history of myocardial infarction were followed through 2004. The multivariable-adjusted relative risks for ever snuff users were 0.91 (95% confidence interval, 0.81-1.02) for nonfatal cases and 1.28 (95% confidence interval, 1.06-1.55) for fatal cases. Heavy users (>or=50 g/day(-1)) had a relative risk of fatal myocardial infarction of 1.96 (95% confidence interval, 1.08-3.58). Snuff use increased the probability of mortality from

cardiovascular disease amongst nonfatal myocardial infarction patients. The results indicate that snuff use is associated with an increased risk of fatal myocardial infarction.

Use of smokeless tobacco and risk of myocardial infarction and stroke: systematic review with meta-analysis. Boffetta P, Straif K. BMJ. 2009 Aug 18;339:b3060. doi: 10.1136/bmj.b3060.

Eleven studies, mainly in men, were included. Eight risk estimates were available for fatal myocardial infarction: the relative risk for ever use of smokeless tobacco products was 1.13 (95% confidence 1.06 to 1.21) and the excess risk was restricted to current users. The relative risk of fatal stroke, on the basis of five risk estimates, was 1.40 (1.28 to 1.54). The studies from both the United States and Sweden showed an increased risk of death from myocardial infarction and stroke. The inclusion of non-fatal myocardial infarction and non-fatal stroke lowered the summary risk estimates. Data on dose-response were limited, but did not suggest a strong relation between risk of dying from either disease and frequency or duration of use of smokeless tobacco products. An association was detected between use of smokeless tobacco products and risk of fatal myocardial infarction and stroke, which does not seem to be explained by chance.

6. Overall Mortality among Smokers who Switched to Spit Tobacco

Tobacco-related disease mortality among men who switched from cigarettes to spit tobacco. Henley SJ, Connell CJ, Richter P, Husten C, Pechacek T, Calle EE, Thun MJ. Tob Control. 2007 Feb;16(1):22-8.

A cohort of 116,395 men was identified as switchers (n = 4443) or cigarette smokers who quit using tobacco entirely (n = 111,952) when enrolled in the ongoing US American Cancer Society Cancer Prevention Study II. From 1982 to 31 December 2002, 44,374 of these men died. The mortality hazard ratios (HR) of tobacco-related diseases, including lung cancer, coronary heart disease, stroke and chronic obstructive pulmonary disease, were estimated using Cox proportional hazards regression modeling adjusted for age and other demographic variables, as well as variables associated with smoking history, including number of years smoked, number of cigarettes smoked and age at quitting.

Results: After 20 years of follow-up, switchers had a higher rate of death from any cause than those who quit using tobacco entirely (HR 1.08, 95% confidence interval (CI) 1.01 to 1.15), lung cancer (HR 1.46, 95% CI 1.24 to 1.73), coronary heart disease (HR 1.13, 95% CI 1.00 to 1.29), and stroke (HR 1.24, 95% CI 1.01 to 1.53).

Conclusion: The risks of dying from major tobacco-related diseases were higher among former cigarette smokers who switched to spit tobacco after they stopped smoking than among those who quit using tobacco entirely.

Scientific Standards for Expressing Toxic Risk for Snuss

Applying toxicological risk assessment principles to constituents of smokeless tobacco products: implications for product regulation, Olalekan A. Ayo-Yusuf and Gregory N. Connolly, Tobacco Control 2011 20: 5357 originally published on line October 5, 2010. (doi: 10. 1136/tc.2010.037135)

This study investigated select STP constituents potentially associated with significant cancer risk by applying a known toxicological risk assessment framework. Cancer risk estimates were obtained for selected constituents of STPs. They also made a medicinal nicotine gum formulation with comparable toxicity information and collected median concentration data on the GothiaTek analytes. The calculated cancer risk was considered 'unacceptable' if it exceeded the US Environmental Protection Agency's (USEPA's) benchmark of an 'acceptable' cancer risk of 10E_6.

The cancer risk estimates derived from daily use of 10 g of STPs were 8,000 times greater than the industry-set GothiaTek limit standard (generally considered acceptable by the USEPA). Except for the medicinal nicotine tested, all the STP types, including the relatively lower tobacco specific nitrosamine (TSNA)-containing snus, were found to carry an unacceptable cancer risk. The calculated cancer risks associated with the snus and the US moist snuff products were, respectively, at least 1000 times and 6000 times greater than the minimum acceptable level. TSNA and cadmium are associated with the largest estimated cancer risks for all the STPs evaluated.

This study's findings provide an empirical risk assessment that could guide STP regulation using an existing toxicological assessment framework. The study findings question the scientific rationale of the industry set standards.

5a. Consumer Response Research

Sampling by consumers of different modalities of smokeless tobacco products may be important in determining appeal of those products. Hatsukami and colleagues demonstrated that smokers showed low preference for General Snus and equal preferences for Camel Snus, Marlboro Snus, Ariva and Stonewall after two weeks of trial. Further research is needed on what product design features of smokeless tobacco products consumers promote appeal among current smokers such as the use of wintergreen in the PRTP applactions, and those intending to quit. Nicotine dosing, additives that provide flavor and other desirable chemosensory effects, ease and convenience of use and brand image may be factors that enhance acceptability among consumers.

5b. Smokeless Tobacco as "Starter" Product for Youth Initiation

The marketing of nicotine addiction by one oral snuff manufacturer

Gregory N. Connolly - Tobacco Control 1995; 4: 73-79.

This article reviews internal industry documents offered into evidence in a 1986 Oklahoma court case, tobacco and advertising industry trade literature, and advertising and promotional material showing how one snuff manufacturer markets nicotine dependence to young people through the design and marketing of low nicotine snuff products.

Smokeless tobacco use increases the risk of young people who start with smokeless tobacco to become smokers and adults are far more likely to switch from smokeless tobacco to cigarette than from cigarettes to smokeless.

Patterns of dual use of cigarettes and smokeless tobacco among U.S. males: findings from national survey, Scott L. Tomar, Hillel R. Alpert and Gregory N. Connolly, Tobacco Control, December 11, 2009 (doi: 10.1136/tc.2009.031070)

This study examined patterns of concurrent use of smokeless tobacco (ST) and cigarettes among young people and adults in the USA immediately prior to cigarette companies' control of the nation's ST market. Data were drawn from four U.S. nationally representative surveys. Stratified analyses applied sampling weights and accounted for the complex sample designs.

Cigarette smoking was substantially more prevalent among young males who used ST than among those who did not. Among adult males, those who smoked daily were less likely than others to have used snuff every day. Men who used moist snuff daily had the lowest prevalence of daily smoking, but the prevalence of daily smoking was relatively high among men who used moist snuff less than daily. Unsuccessful past-year attempts by daily smokers to quit smoking were more prevalent among non-daily snuff users (41.2%) than among those who had never used snuff (29.6%).

Although dual daily use of ST and cigarettes is relatively uncommon in the USA, concurrent ST use is more common among adolescent and young adult male smokers than among more mature tobacco users. Among adult males, daily smoking predominates and non-daily ST use is very strongly associated with current smoking. Adult male smokers who also use ST daily tend to have relatively high levels of serum cotinine and high prevalence of a major indicator for tobacco dependence.

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SWEDISH MATCH

2009-02-03

Professor Gregory N. Connolly
Harvard School of Public Health
677 Huntington Avenue
Landmark Center
Boston, MA 02115

Dear Professor Connolly,

Re: Request for scientific data

Thank you for your letter addressed to the CEO of Swedish Match AB Mr Lars Dahlgren. He has asked me to provide you with our response.

Swedish Match is committed to have an open relationship with the scientific community and representatives of the public health sector. We believe that transparency regarding relevant scientific evidence is in the best interest ofthe public as well as the industry. We also strongly sympathize with actions that promote science in the field of smokeless tobacco and welcome efforts to develop an evidence-based public health response.

As you are probably well aware, your request for scientific data supporting specific levels of toxins in smokefree tobacco products concerns complex issues in many scientific areas. Our voluntary GothiaTek standard, for instance, was developed over several years taking into account both practical and scientific considerations relating to our products. This standard formed the basis for the proposal from ESTOC (the European trade organisation for producers of smokefree tobacco products) to the European Union for a regulation of smokefree tobacco products. We agree with those who feel that much could be gained from a more unified vision and strategy to guide research and policy in the area of tobacco product regulation.

Our possibilities to address the issues you bring up in your letter would be much improved if you could let us know more details on the background, scope and purpose of your request. For instance, we would appreciate very much to see the protocol for the research for which you need these data.

Sincerely,

Lars E. Rutqvist, M.D., Ph. D.
Senior Vice President Scientific Affairs
Swedish Match AB
SE-118 85, Stockholm
SWEDEN

Cc: Lars Dahlgren, CEO,

HARVARD SCHOOL OF PUBLIC HEALTH
Division of Public Health Practice
Translating passion and learning into advances that protect the health of all

February 3, 2009

Mr. Lars Dahlgren
President and Chief Executive Officer
Swedish Match
Corporate Headquarters
SE-118 85 Stockholm
Fax: +46 8 658 3522

Dear Mr. Dahlgren:

It is our understanding that Swedish Match has adopted the Gothia Standard for setting levels of toxins in its smokeless tobacco products. We are conducting research in this area and would appreciate your company's scientific data for setting such levels including but not limited to risk assessments done for each chemical by recognized health and safety agencies and in vitro and in vivo studies showing that such levels reduce risk of disease compared to products with high levels.

If you have any questions with regard to the request, you can reach me at gconnoll@hsph.harvard.edu.

Sincerely,

(b) (6)

Gregory N. Connolly, D.M.D., M.P.H.

Mailing Address: 677 Huntington Avenue, Landmark Center, Boston, MA 02115
Location Address: Landmark Center, 401 Park Drive, 3rd Floor East, Boston, MA 02215
Phone: (617) 496-0863 Fax: (617) 495-8543

Smokeless Product	Manufacturer	Sample Origin	Date of shipment	Nicotine dry weight* (µg/g)		Nicotine Wet Wt (Conversion) (mg/g)		Free-base Nicotine (%)
Labstat 2006				**Average**	**St Dev**	**Average**	**St Dev**	
Grizzly Fine Cut Natural	Conwood	Massachusetts	10/5/2006	28362	1032	12.81	0.47	49.3
Grizzly Long Cut Straight	Conwood	Massachusetts	10/5/2006	21746	560	10.03	0.26	43.3
Grizzly Long Cut Wintergreen	Conwood	Massachusetts	10/5/2006	18657	671	8.72	0.31	62.8
Kodiak Wintergreen	Conwood	Massachusetts	10/5/2006	19606	510	9.02	0.23	79.2
Kodiak Ice	Conwood	Massachusetts	10/5/2006	18797	205	8.52	0.09	57.9
Hawken Wintergreen	Conwood	Massachusetts	10/5/2006	5574	90	4.05	0.07	0.1
Copenhagen Long Cut	US Tobacco	Massachusetts	10/5/2006	27325	817	12.57	0.38	34.0
Copenhagen Snuff	US Tobacco	Massachusetts	10/5/2006	24622	896	11.46	0.42	16.6
Copenhagen Pouches	US Tobacco	Massachusetts	10/5/2006	23154	358	14.19	0.22	11.6
Skoal Long Cut Straight	US Tobacco	Massachusetts	10/5/2006	27550	660	12.53	0.30	28.3
Skoal Long Cut Apple	US Tobacco	Massachusetts	10/5/2006	24423	1662	10.94	0.74	51.6
Skoal Long Cut Wintergreen	US Tobacco	Massachusetts	10/5/2006	28047	335	12.69	0.15	24.4
Skoal Bandits Mint	US Tobacco	Massachusetts	10/5/2006	17587	1070	9.15	0.56	7.0
Skoal Bandits Straight	US Tobacco	Massachusetts	10/5/2006	20425	220	10.59	0.11	0.3
Red Seal Natural Flavor Fine Cut	US Tobacco	Massachusetts	10/5/2006	28932	514	13.03	0.23	22.2
Timber Wolf Natural Fine Cut	Swedish Match	Massachusetts	10/5/2006	30513	969	14.81	0.47	36.0
Timber Wolf Fine Cut Peach	Swedish Match	Massachusetts	10/5/2006	26716	607	12.92	0.29	7.0
Longhorn Fine Cut Natural	Swedish Match	Massachusetts	10/5/2006	27553	860	13.25	0.41	26.5
Redwood Fine Cut Snuff	Swisher	Massachusetts	10/5/2006	26875	722	12.77	0.34	4.6
Kayak Long Cut Wintergreen	Swisher	Massachusetts	10/5/2006	23738	217	12.42	0.11	6.5
Cooper Wintergreen Long Cut	Swisher	Massachusetts	10/5/2006	15577	260	8.03	0.13	7.9
Taboka Original	Philip Morris	Indianapolis, IN	10/5/2006	13917	138	12.66	0.13	3.1
Camel Snus Original (Oregon)	Reynolds	Portland, OR	10/5/2006	21274	760	14.47	0.52	17.1
Camel Snus Original (Texas)	Reynolds	Austin, TX	10/5/2006	20878	478	14.00	0.32	16.6
Grizzly Fine Cut Natural	Conwood	Massachusetts	7/23/2007	30761	578	13.93		29.9
Grizzly Long Cut Straight	Conwood	Massachusetts	7/23/2007	27006	464	12.42		40.3
Grizzly Long Cut Wintergreen	Conwood	Massachusetts	7/23/2007	24436	82	11.46		54.0
Kodiak Wintergreen	Conwood	Massachusetts	7/23/2007	21383	1239	9.77		74.3
Kodiak Ice	Conwood	Massachusetts	7/23/2007	24824	635	11.22		70.1
Hawken Wintergreen	Conwood	Massachusetts	7/23/2007	4650	86	3.28		0.2

BOBCAT Fine Cut Straight	American Smokeless	Massachusetts	9/28/2007	21419	534	8.97	76.5
COUGAR Long Cut NATURAL	Conwood	Massachusetts	9/28/2007	19318	1223	8.85	67.4
BOBCAT Fine Cut Wintergreen	American Smokeless	Massachusetts	9/28/2007	19070	1115	8.69	13.1
COUGAR SNUFF	Conwood	Massachusetts	9/28/2007	19489	677	9.01	43.0
SILVER CREEK Long Cut Wintergreen	Swisher	Massachusetts	9/28/2007	17163	440	7.89	6.0
GOLD RIVER Long Cut	Swisher	Massachusetts	9/28/2007	11613	358	8.70	0.5
SILVER CREEK Fine Cut Wintergreen	Swisher	Massachusetts	9/28/2007	22978	534	10.62	16.8
COOPER Long Cut Wintergreen	Swisher	Massachusetts	9/28/2007	13775	630	6.48	7.0
HUSKY Fine Cut Natural Flavor	US Tobacco	Massachusetts	9/28/2007	28276	633	12.54	30.0
LONGHORN Fine Cut Natural	Pinkerton	Massachusetts	9/28/2007	26241	1268	12.62	37.1
HUSKY Fine Cut Wintergreen	US Tobacco	Massachusetts	9/28/2007	27863	561	12.76	25.2
LONGHORN Fine Cut Wintergreen	Pinkerton	Massachusetts	9/28/2007	30527	1910	14.03	34.8
Marlboro SNUS Rich	Philip Morris	Dallas	12/20/2007	14050	63	12.42	4.9
Marlboro SNUS Mild	Philip Morris	Dallas	12/20/2007	14721	240	13.21	3.4
Marlboro SNUS Spice	Philip Morris	Dallas	12/20/2007	14401	283	12.75	8.7
Marlboro SNUS Mint	Philip Morris	Dallas	12/20/2007	13981	151	12.52	6.2
Marlboro Fine Cut Original	Philip Morris	Atlanta	12/20/2007	27238	557	12.49	31.0
Marlboro Long Cut Original	Philip Morris	Atlanta	12/20/2007	25816	658	11.82	27.9
Marlboro Fine Cut Wintergreen	Philip Morris	Atlanta	12/20/2007	27416	966	12.56	24.0
Marlboro Long Cut Wintergreen	Philip Morris	Atlanta	12/20/2007	24880	177	11.56	28.9

Free-base Nicotine mg/g	Total TSNA	NNN* (ng/g)		NNN Wet Wt (ng/g)				NAT Wet Wt (ng/g)			
		Average	St Dev	Average	St Dev	Average	St Dev	Average	St Dev	Average	St Dev
6.32	22750	14771	300	6674	136	29585	655	13367	296	2229	72
4.35	9666	7632	246	3521	113	10063	367	4642	169	684	66
5.47	7508	6461	325	3018	152	7229	398	3377	186	529	53
7.14	9215	6716	374	3090	172	9686	608	4457	280	681	36
4.93	5184	4814	102	2183	46	5158	73	2338	33	457	45
0.0045	4169	3171	16	2304	11	1400	39	1018	28	203	21
4.27	5623	5982	151	2752	70	3991	111	1836	51	402	37
1.91	5435	5393	323	2510	150	4495	338	2092	157	347	29
1.64	6413	5193	60	3183	37	3786	68	2321	42	301	13
3.55	5176	5429	131	2469	60	3950	161	1797	73	353	24
5.65	4391	4691	105	2101	47	3382	49	1515	22	259	24
3.09	5982	6647	67	3007	30	4166	90	1885	41	331	13
0.64	9496	9632	446	5014	232	4924	238	2563	124	311	23
0.03	3254	3414	86	1770	44	2196	130	1139	67	NQ	NQ
2.89	4922	5242	339	2361	153	4192	263	1888	118	313	14
5.33	5605	4848	139	2353	67	5301	86	2574	42	345	22
0.91	4220	3744	220	1811	106	3778	174	1827	84	274	25
3.51	5235	4234	29	2036	14	5568	118	2678	57	341	13
0.59	14885	10306	567	4897	269	16471	946	7826	449	1109	42
0.81	15546	10727	469	5614	245	11934	501	6246	262	1208	74
0.63	22905	15143	874	7806	450	20228	1214	10428	626	2023	112
0.39	1398	826	45	752	41	710	46	646	41	NQ	NQ
2.47	1336	1116	61	759	42	848	41	577	28	NQ	NQ
2.33	1435	1245	15	835	10	896	16	601	11	NQ	NQ
4.17	15082	11558		5236		16405		7431		802	
5.01	6778	5019		2309		7758		3569		435	
6.19	5598	4937		2315		5599		2626		376	
7.26	11148	8977		4102		12895		5893		678	
7.87	7465	6719		3037		7344		3319		490	
0.0067	3908	3144		2217		1282		904		193	

6.87	287647	338007	10674	141613	4472	320892	6831	134442	20586	235
5.96	4943	5033	69	2305	31	4064	145	1861	339	12
1.14	2050	2998	11	1366	5	1501	25	684	BDL	BDL
3.88	4077	4087	54	1890	25	3106	38	1436	268	22
0.47	12655	8985	315	4131	145	13812	710	6349	1089	90
0.04	1777	1524	28	1142	21	847	20	635	NQ	NQ
1.79	5529	4816	24	2226	11	4561	62	2108	481	35
0.45	11856	8571	225	4033	106	12037	351	5664	1018	66
3.76	5167	5648	43	2505	19	4029	143	1787	339	31
4.68	5460	4372	64	2102	31	5278	92	2538	327	30
3.21	4676	4933	60	2259	27	3670	109	1681	331	22
4.88	3913	3532	42	1623	20	3765	90	1730	266	18
0.61		546	13			545	24		BDL	BDL
0.45		723	17			650	25		BDL	BDL
1.12		632	16			597	34		BDL	BDL
0.78		765	38			695	35		NQ	NQ
3.87		7035	65			5478	97		658	14
3.30		7848	224			5946	209		771	56
3.02		7286	114			5922	128		707	13
3.35		7469	36			5678	104		692	24

NAB Wet Wt (ng/g)				NNK Wet Wt (ng/g)	pH Result		Dry Matter (%)		Moisture (%)	
Average	St Dev	Average	St Dev	Average	Average	St Dev	Average	St Dev	Average	St Dev
1007	32	3767	163	1702	8.01	0.02	45.2	0.2	54.8	0.2
316	30	2573	73	1187	7.90	0.01	46.1	0.2	53.9	0.2
247	25	1853	108	866	8.25	0.02	46.7	0.1	53.3	0.1
313	17	2946	191	1355	8.60	0.02	46.0	0.1	54.0	0.1
207	21	1005	72	456	8.16	0.01	45.3	0.0	54.7	0.0
148	16	962	31	699	5.06	0.01	72.7	0.2	27.3	0.2
185	17	1851	53	851	7.73	0.01	46.0	0.2	54.0	0.2
162	13	1442	111	671	7.32	0.00	46.5	0.1	53.5	0.1
184	8	1184	25	725	7.14	0.00	61.3	0.1	38.7	0.1
160	11	1648	155	750	7.62	0.01	45.5	0.1	54.5	0.1
116	11	1471	92	659	8.05	0.01	44.8	0.1	55.2	0.1
150	6	2080	107	941	7.53	0.01	45.2	0.0	54.8	0.0
162	12	3375	159	1757	6.90	0.01	52.1	0.1	47.9	0.1
NQ	NQ	665	50	345	5.50	0.00	51.9	0.0	48.1	0.0
141	6	1181	55	532	7.48	0.00	45.0	0.1	55.0	0.1
168	11	1051	54	510	7.77	0.01	48.5	0.1	51.5	0.1
132	12	930	61	450	6.90	0.00	48.4	0.2	51.6	0.2
164	6	741	26	356	7.58	0.01	48.1	0.2	51.9	0.2
527	20	3440	259	1634	6.71	0.01	47.5	0.2	52.5	0.2
632	39	5835	195	3054	6.86	0.00	52.3	0.0	47.7	0.0
1043	58	7037	380	3628	6.95	0.01	51.6	0.4	48.4	0.4
NQ	NQ	BDL	BDL	NQ	6.52	0.01	90.9	0.1	9.05	0.06
NQ	NQ	NQ	NQ	NQ	7.33	0.01	68.0	0.3	32.0	0.3
NQ	NQ	NQ	NQ	NQ	7.32	0.01	67.0	0.3	33.0	0.3
363		4528		2051	7.65		45.3		54.7	
200		1523		701	7.85		46.0		54.0	
176		1023		480	8.09		46.9		53.1	
310		1843		842	8.48		45.7		54.3	
221		1962		887	8.39		45.2		54.8	
136		924		651	5.33		70.5		29.5	

8625	7082	188	2967	8.53	0.01	41.9	58.1
155	1358	43	622	8.34	0.01	45.8	54.2
0	NQ	NQ	0	7.20	0.02	45.6	54.4
124	1356	23	627	7.90	0.03	46.2	53.8
501	3642	122	1674	6.82	0.01	46.0	54.0
0	NQ	NQ	0	5.72	0.01	74.9	25.1
222	2105	24	973	7.33	0.01	46.2	53.8
479	3571	146	1680	6.90	0.02	47.1	52.9
151	1636	33	725	7.65	0.02	44.3	55.7
157	1378	25	663	7.79	0.01	48.1	51.9
151	1278	40	585	7.55	0.01	45.8	54.2
122	952	34	438	7.75	0.02	46.0	54.0
	NQ	NQ		6.74	0.01	88.4	11.6
	NQ	NQ		6.57	0.05	89.7	10.3
	NQ	NQ		7.00	0.02	88.6	11.4
	NQ	NQ		6.84	0.04	89.5	10.5
	2208	40		7.67	0.03	45.9	54.1
	2390	97		7.61	0.05	45.8	54.2
	2622	50		7.52	0.02	45.8	54.2
	2221	59		7.63	0.07	46.5	53.5